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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/612,393	07/03/2003	Thomas E. Tarara	16614-030001	3183

26181 7590 08/01/2006

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EXAMINER	
GOLLAMUDI, SHARMILA S	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 08/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/612,393	TARARA ET AL.	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-28* is/are pending in the application.

4a) Of the above claim(s) *2-23,27 and 28* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt Request for Continued Examination, Amendments/Remarks, and Information Disclosure Statement filed on 5/10/06 is acknowledged. Claims **24-26** are pending in this application. Claims 1-23 and 27-28 are withdrawn as being directed to a non-elected invention.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/10/06 has been entered.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 5/10/06 has been considered by the examiner. The information disclosure statement filed 11/9/06 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. Note the IDS has been considered, only *certain* NPL documents that have not been submitted and or illegible have not been considered by the examiner.

Priority

With regard to claim 24 and 26, applicant is entitled the priority claim of provisional application 60/060337 with a filing date of 9/29/97. However, the subject matter of claim 25

does not does not have support in provisional application 60/060337 and thus is not entitled the priority claim to 9/29/97. With regard to claim 25, ammonium acetate and ammonium carbonate are entitled to the effective filing date of 9/29/98.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 24 and 26 rejected under 35 U.S.C. 102(e) as being anticipated by Sutton et al (5,993,805).

Sutton discloses spray-dried microparticles, which carry a therapeutic or diagnostic agent and method spray drying a composition to provide the microparticles. See abstract. The microsphere are characterized as hollow microspheres with proteinaceous walls, which are 1.0-8.0 microns in diameter, and have a wall thickness of 100-500 nm. See column 5, lines 40-47.

Sutton discloses a process for preparing microcapsules comprising atomizing a solution (or dispersion) of a wall-forming material. The therapeutic or diagnostic agent may be atomized therewith, or coupled to the microcapsules. Alternatively, the wall forming material may be an active agent itself. Generally, the wall-forming material may be selected from polysaccharides of low water solubility, polylactides and polyglycolides and their copolymers, copolymers of lactides and lactones, polypeptides, and proteins such as gelatin, collagen, globulins and albumins. See column 6, lines 10-60.

Example 12 teaches dissolving 500 mg beclomethasone (therapeutic active) in ethanol and it to 50 ml HAS (albumin) feedstock (10% w/v) and spray-dried using the conditions outlined in Example 10. Sutton teaches the use of ethanol provides particles that are smooth and spherical. See column 17, lines 55-57. Note ethanol which has a boiling point 78.3.degree. C. and reads on the "blowing agent" as defined by instant specification on page 27, lines10-12.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sutton et al (5,993,805) in view of Roberts (4999384) or US 2,797,201 to Veatch.

Sutton teaches spray-dried microparticles which carry a therapeutic or diagnostic agent and method spray drying a composition to provide the microparticles. See abstract. The

microsphere are characterized as hollow microspheres with proteinaceous walls, which are 1.0-8.0 microns in diameter, and have a wall thickness of 100-500 nm. See column 5, lines 40-47.

Sutton teaches a process for preparing microcapsules of the invention comprises atomizing a solution (or dispersion) of a wall-forming material. The therapeutic or diagnostic agent may be atomized therewith, or coupled to the microcapsules. Alternatively, the wall forming material may be an active agent itself. Generally, the wall-forming material may be selected from polysaccharides of low water solubility, polylactides and polyglycolides and their copolymers, copolymers of lactides and lactones, polypeptides, and proteins such as gelatin, collagen, globulins and albumins. See column 6, lines 10-60.

Example 12 teaches dissolving 500 mg beclomethasone in ethanol and it to 50 ml HAS (albumin) feedstock (10% w/v) and spray-dried using the conditions outlined in Example 10. Sutton teaches the use of ethanol provides particles that are smooth and spherical. See column 17, lines 55-57. Note ethanol which has a boiling point 78.3.degree. C. and reads on the "blowing agent" as defined by instant specification on page 27, lines10-12.

Sutton does not teach the use the instantly claimed blowing agent.

Roberts teaches polycarbonate resin/polyamide resin blend composition, which is expanded to form a porous cellular, solidified structure by the action of various propellants or agents for expanding or blowing the materials. The blowing agents, in accordance with *common practice*, are usually gases, gas generating solids, or highly fugacious liquids. The blowing agents include gases which expand upon the release of pressure to foam the resin composition, liquids while will vaporize to a gas and expand the resin upon the release of pressure, solids which decompose to release a gas, and combinations of such gases, liquids, and solids. Examples

of suitable normally gaseous agents include paraffins such as propane or butane and more permanent gases such as nitrogen, carbon dioxide, and air. Similarly, olefins such as ethylene, propylene, butylene, etc., and mixtures thereof. Suitable conventional liquid blowing agents include methyl chloride, higher paraffins such as pentane or hexane, fluorocarbons, etc. Examples of suitable solids which upon decomposition release a gas are ammonium or azo type compounds, such as ammonium carbonate, ammonium bicarbonate, potassium bicarbonate, diazoaminobenzene, diazoaminotoluene, azodicarbonamide, diazoisobutyronitrile, etc. Alcohol blowing agents include isopropanol, ethanol and methanol. See column 3, lines 15-56.

Veatch et al disclose a spray drying process of producing hollow particles. The film forming material may be a natural material such as proteins, alginates, and celluloses. See column 3, lines 23-30. Veatch teaches a number of blowing agents are known in the art and the blowing agent may be a liquid or solid that volatizes or a substance that decomposes to form a gas. Veatch teaches suitable decomposable blowing agents are inorganic/organic salts such as ammonium carbonate. Veatch also teaches methyl ethyl ketone may be used instead of acetone as the blowing agent. See column 2, lines 1-55 and examples.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teaching of Sutton et al and Roberts et al and utilize the instantly claimed blowing agent in the spray solution. One would have been motivated to substitute the prior art's blowing agent ethanol with the instantly claimed blowing agent with the expectation of similar results since Roberts teaches the method of spraying drying hollow particles using volatile type blowing agent such as ethanol (evaporation type) or a decomposing type blowing agents such as ammonium salts. Thus, it would have prima facie obvious, absent the showing of

unexpected results of the instantly claimed blowing agents, to utilize any blowing agent known in the art to produce the hollow microspheres. Further, a skilled artisan would have expected success since Roberts teaches that both ethanol and instant ammonium salts have the same function and purpose, i.e. act as expanding agents to provide porous spheres. It is noted that Roberts is directed to making foamed sheets comprising foamed microparticles and Sutton is directed to diagnostic/therapeutic microparticles; however the examiner points out that Roberts demonstrates the state of art wherein the instantly claimed blowing agents are known and utilized in the art to produce porous microspheres. Moreover, the function of the blowing agent would remain the same (the function of expanding the particle to be porous would not change) regardless of the type and intended use of the microparticle produced.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teaching of Sutton et al and Veatch and utilize the instantly claimed blowing agent in the spray solution. One would have been motivated to substitute the prior art's blowing agent with the instantly claimed blowing agent with the expectation of similar results since Veatch teaches the method of spraying drying hollow particles may utilize a volatile type blowing agent (evaporation type) or a decomposing type blowing agents such as ammonium salts. Thus, it would have prima facie obvious, absent the showing of unexpected results of the instantly claimed blowing agents, to utilize any blowing agent known in the spray drying art, i.e. a decomposing type versus an evaporation type, to produce the hollow microspheres.

Claims 24 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 92/18164 to Sutton et al in view of WO 96/15814 to Osborne et al.

Sutton teaches a process of preparing microcapsules comprising the steps of (i) spray-drying a solution or dispersion of a wall-forming material in order to obtain intermediate microcapsules and (ii) reducing the water-solubility of at least the outside of the intermediate microcapsules. The microcapsules have walls of 40-500 nm thick and 1-50 microns diameter, which are useful in ultrasonic imaging. See abstract. The wall-forming material is proteinaceous, for example, it may be collagen, gelatin or (serum) albumin. See page 6, lines 9-16. The solution contains 0.1-50% and preferably 5-25% of the protein. See page 7, lines 18-23. Sutton teaches the preparation to be sprayed may contain substances other than the wall-forming material and solvent or carrier liquid. See page 7, lines 25-28.

Sutton teaches the microspheres are for imaging a wide variety of areas including:(1) the venous drainage system to the heart; (2) the myocardial tissue and perfusion characteristics during an exercise treadmill test or the like; and (3) myocardial tissue after an oral ingestion or intravenous injection of drugs designed to increase blood flow to the tissue. Additionally the microspheres may be useful in delineating changes in the myocardial tissue perfusion due lo interventions such as (1) coronary artery vein grafting; (2) coronary artery angioplasty (balloon dilation of a narrowed artery); (3) use of thrombolytic agents (such as streptokinase) to dissolve clots in coronary arteries; or (4) perfusion defects or changes due to a recent heart attack. See page 20.

Although Sutton teaches the use of additives in the spray drying solution, Sutton does not specify the use of a blowing agent or a bioactive agent as the additive in the spray drying solution.

Osborne teaches process for forming microcapsules comprising (i) providing a solution of a protein in an aqueous solvent and (ii) spraying the said solution into a gas such that the aqueous solvent evaporates, thereby forming hollow microcapsules, characterized in that the aqueous solution contains a liquid of greater volatility than water. The microcapsules are useful for ultrasound imaging. See abstract. Suitable volatile liquids include ethanol (boiling point 78.3.degree. C.), methanol (b.p. 64.5.degree. C.), and acetone (b.p. 56.degree. C.). Note that these volatile liquid solvents reads on the "blowing agent" as defined by instant specification on page 27, lines10-12. See page 2, lines 5-10. Osborne teaches that including a volatile compound in the aqueous solution, which is spray-dried, microcapsules with improved properties can be formed, in higher yield, with narrower size distribution and thinner shells. See page 1, lines 24-26. The aqueous solution (feedstock) contains a wall-forming material, which is a water-soluble material, preferably a protein, including collagen, gelatin or (serum) albumin. See page 3, lines 3-15. Osborne teaches functional agents may be included in the solution, for example at 1.0-40.0% w/w, such as X-ray contrast agents or magnetic resonance imaging agents (ioxalic, ivorsol, iohexol, iron oxide, iopamidol, gadolinium). See page 4, lines 15-20.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teaching of Sutton et al and Osborne et al and utilize a blowing agent, i.e. Osborne's volatile solvent, in Sutton's spray solution. One would have been motivated to do so since Osborne teaches the inclusion of a volatile compound in the aqueous solution ,which is spray-dried, provide microcapsules with improved properties that can be formed in higher yield, with narrower size distribution and thinner shells. Thus, a skilled artisan would have been motivated to further add a blowing agent in the spray dry solution to increase the number of

hollow microcapsules yielded by the process and to produce microcapsules with improved properties. Further, a skilled artisan would have expected success by the instant combination since Sutton teaches the use of a solvent in the spray solution and both references are directed to a method of making hollow microcapsules that are used for ultrasound. Secondly, one would have been motivated to add a bioactive agent such as a contrast agent or magnetic resonance imaging agent to the spray solution. A skilled artisan would have been motivated to do so since Sutton teaches the microcapsules are utilized for imaging areas in the body and the inclusion of a contrast agent or a magnetic resonance imaging agent would further enhance the imaging process.

Response to Arguments

Applicant argues that the use of a contrast agent or imagining agent is not a bioactive agent. Applicant argues that while these agents enable a scanner to image the agent within the body, these agents are not necessarily bioactive.

Applicant's arguments filed 5/10/06 have been fully considered but they are not persuasive. The examiner notes page 19 of the instant specification, which discloses:

> Compatible **bioactive agents** comprise hydrophilic and lipophilic respiratory agents, pulmonary surfactants, bronchodilators, antibiotics, antivirals, anti-inflammatories, steroids, antihistamines, leukotriene inhibitors or antagonists, anticholinergics, antineoplastics, anesthetics, enzymes, cardiovascular agents, genetic material including DNA and RNA, viral vectors, immunoactive agents, **imaging agents**, vaccines, immunosuppressive agents, peptides, proteins and combinations thereof. Particularly preferred bioactive agents for inhalation therapy comprise mast cell inhibitors (anti-allergics), bronchodilators, and anti-inflammatory steroids such ms, for example, cromoglycate (e.g. the sodium salt), and albuterol (e.g. the sulfate salt). (Emphasis made by examiner).

Thus, it is clear that imaging agents such as those taught by the prior art are considered "bioactive agents".

Secondly, the examiner agrees with applicant's assertion that there is a difference between "therapeutic" and "diagnostic". However, it is noted that the secondary reference,

Osborne et al, teach functional agents such as iron oxide and gadolinium. The examiner points out that both iron oxide and gadolinium have dual functions of serving as a diagnostic *and* therapeutic agent. The examiner cites US 5,260,050 (column 50, line 44-66):

> For the various metal atoms described above, it is emphasized here that numerous **different metals may serve as either or both diagnostic or therapeutic agents** (including.sup.(195) platinum, **gadolinium**, boron, gold and others). Hence, they are included together in the present application, and are considered all to be variations of a single, unified approach to preparing compositions of matter involving (polyatomic or other) metal-atom-complex carriers. In terms of various pharmaceutical applications, platinum is used as a chemotherapeutic as well as potentially a paramagnetic agent for MRI diagnosis; and boron and boroleptics (boron complexes) can be used either as therapeutic radiation enhancers or as diagnostic agents, as can gold salts. Gold salts and metal-atom coordinates (including, among others, the therapeutic antiinflammatory/antiarthritic agent Auraofin.TM.) can be administered for therapeutic purposes by formulating these salts (coordinates) as the metal-atom complexes described above. Hence, the single nature and structural category of these metal-atom-carrier compositions is apparent and supported in a fashion independent of their potentially multiple diagnostic and therapeutic pharmaceutical indications (Emphasis made by examiner).

US 5,427,767 (column 4, lines 40-55) is also cited:

> The therapeutic benefit of the aforesaid iron oxide particles is based on the applicability of iron preparations as anti-anemic drugs as well as in magnetic targeting, a possibility of targeted transport of iron oxide particles and adhering substances to the site of action by means of external magnetic fields.

Thus, it can be seen that Osborne's functional agents read on the instantly claimed "therapeutic bioactive agent" since certain imaging agents have both therapeutic and diagnostic properties.

Claim 25 is rejected under 35 U.S.C. 103(a) as being unpatentable over WO 92/18164 to Sutton et al in view of WO 96/15814 to Osborne et al in further view of 2,797,201 to Veatch.

The teachings of Sutton et al and Osborne et al have been delineated above. Sutton teaches a method pf spray drying microcapsules for ultrasound that have a wall thickness of 45-500nm. Osborne teaches microcapsules with thin shells for ultrasound, which are made by spray drying using a volatile solvent, which is a blowing agent that evaporates.

The references do not teach the instantly claimed blowing agent.

Veatch et al disclose a spray drying process of producing hollow particles. The film forming material may be a natural material such as proteins, alginates, and celluloses. See column 3, lines 23-30. Veatch teaches a number of blowing agents are known in the art and the blowing agent may be a liquid or solid that volatizes or a substance that decomposes to form a gas. Veatch teaches suitable decomposable blowing agents are inorganic/organic salts such as ammonium carbonate. Veatch also teaches methyl ethyl ketone may be used instead of acetone as the blowing agent. See column 2, lines 1-55 and examples.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teaching of Sutton et al, Osborne et al, and Veatch and utilize the instantly claimed blowing agent in the spray solution. One would have been motivated to substitute the prior art's blowing agent with the instantly claimed blowing agent with the expectation of similar results since Veatch teaches the method of spraying drying hollow particles may utilize a volatile type blowing agent (evaporation type) or a decomposing type blowing agents such as ammonium salts. Thus, it would have prima facie obvious, absent the showing of unexpected results of the instantly claimed blowing agents, to utilize any blowing agent known in the spray drying art, i.e. a decomposing type versus an evaporation type, to produce the hollow microspheres.

Response to Arguments

Applicant argues that Veatch describes making hollow particles for low-density products such as floor tiles, plaster, plastic foam, deals, boat hull, and other items. Applicant argues that

Veatch does not suggest a therapeutic agent and thus does not cure the deficiency of Sutton and Osborne.

Applicant's arguments filed 5/10/06 have been fully considered but they are not persuasive. Firstly, the examiner points out that all three references are directed to making hollow particles for various uses and although Veatch does not specify using the particles for therapeutic purposes, the examiner points out that the method of spray drying remains the same regardless of the type and intended use of the particle produced. Thus, the references are considered to be in the same field of endeavor, i.e. process of spray drying hollow microspheres. Secondly as discussed above, it is the examiner's position that the rejection over Sutton in view of Osborne does not lack the teaching of a therapeutic agent. Therefore, Veatch is not relied upon to teach a therapeutic agent since Sutton and Osborne are not deficient in this sense. Veatch is relied upon to teach the use of a blowing agent and applicant has not provided any evidence to overcome the prima facie obviousness rejection.

Claims 24-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grimm III (3,957,964) in view of US patent 4,180,593 to Cohan et al or vice-versa.

Grimm teaches dentrifice capsules that encapsulate flavoring material. See abstract. Grimm also teaches the encapsulation of fluorides, antibiotics, bactericides and colorants which can be released in active form. See column 2, lines 10-12. Grimm teaches that by regulating capsule wall thicknesses and sizes, an even release of bursts of the same or different flavors and colors may be effected during use of the dentifrices. Grimm teaches the capsules will be substantially spherical or of rounded cube shape with a diameter or equivalent diameter in the one micron to 2 millimeters range, preferably in the range of 50 microns to 1 millimeter and

especially from 500 to 800 microns. The thicknesses of the walls of the capsules range from 0.1 micron (100 nm) to 1 millimeter. Grimm teaches the thickness prevents premature breaking of the capsules. See column 5, lines 1-10. Grimm teaches various encapsulation processes, of which aqueous phase separation, interfacial polymerization, multi-orifice rotating cylinder, fluidized bed spray coating, melt prilling in a fluidized bed, spray drying, etc. See column 4, lines 3-10. The film forming material (wall forming) may be selected from gelatin and organic gums. See column 3, line 58.

Although Grimm suggests the capsules may be formed by spray drying, Grimm does not specify the method of forming the capsules, i.e. using a blowing agent.

Cohan et al teach a process of producing round spherical free flowing blown beads of controlled bulk density for food products. See abstract. The process includes providing a sprayable composition, which includes an edible film, a liquid, and a blowing agent (ammonium salts: carbonate and bicarbonate). The particles are spray-dried to produce the spherical beads. See examples, column 1, lines 50-60, and column 4. The blowing agent upon exposure to the elevated temperatures in the heated zone will form a gas in situ to expand the solution. Suitable film materials include carbohydrates such as the dextrins, starch, pectin, algin, methyl cellulose, carboxy methyl cellulose, carboxy methyl amylose, carboxy methyl amylopectin, dextrose, fructose, maltose, lactose, and dextrans, natural gums such as tragacanth, acacia, arabic, locust bean, caraya, and carragean. Cohan teaches the particles provide a low bulk density carrier and preferably are used to encapsulate a flavor such as coffee (note coffee contains caffeine which reads on the instant "bioactive agent), chocolate, and tea; colors; or sweetening agents. Suitable sweeteners include natural sweeteners such as fructose, sucrose, invert sugar, honey,

polysaccarides, extracts from orange and grapefruit peels, and artificial sweeteners including cyclamates, saccharin, and aspartame. See column 2, lines 15-45.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teaching of Grimm and Cohan et al and utilize Cohan's process of spray drying to form the encapsulating capsules. One would have been motivated to do so with the expectation of similar results since Grimm teaches any suitable process may be utilized to form the capsules including spray drying and Cohan demonstrates the state of the art at the time the invention was made wherein it is known to incorporate a blowing agent in the spray drying solution to yield spherical, light particles.

Conversely ,it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teaching of Cohan et al and Grimm and make a particle with the instant wall thickness since Cohan does not specify the wall thickness of the blown beads. One would have been motivated to do so since Grimm teaches the manipulation of the wall thickness provides effects the "burst" effect to the encapsulated material. Thus, a skilled artisan would have been motivated to manipulate the wall thickness depending on the desired release of the capsule contents. A skilled artisan would have expected similar results since both Cohan et al and Grimm are directed to encapsulating shells.

Response to Arguments

Applicant argues Grimm and Cohan fail to teach or suggest a therapeutic bioactive agent. Applicant argues that Grimm suggests forming the capsules having antibiotics in a polymeric plastic to keep the unstable active from being exposed to the surrounding environment. Applicant argues that to put the antibiotic in a coating would counter Grimm's purpose. Applicant argues a

modification that counters the purpose of the prior art and thus is improper. Applicant argues Cohan does not teach a therapeutic bioactive agent.

Applicant's arguments filed 5/10/06 have been fully considered but they are not persuasive. The examiner notes page 19 of the instant specification, which discloses:

> Compatible **bioactive agents** comprise hydrophilic and lipophilic respiratory agents, pulmonary surfactants, bronchodilators, **antibiotics**, antivirals, anti-inflammatories, steroids, antihistamines, leukotriene inhibitors or antagonists, anticholinergics, antineoplastics, anesthetics, enzymes, cardiovascular agents, genetic material including DNA and RNA, viral vectors, immunoactive agents, imaging agents, vaccines, immunosuppressive agents, peptides, proteins and combinations thereof. Particularly preferred bioactive agents for inhalation therapy comprise mast cell inhibitors (anti-allergics), bronchodilators, and anti-inflammatory steroids such ms, for example, cromoglycate (e.g. the sodium salt), and albuterol (e.g. the sulfate salt). (Emphasis made by examiner).

Thus, it is clear that antibiotics such as those taught by the prior art are considered "bioactive agents".

Applicant's argument with regard to encapsulation is unclear. The examiner points out that wall forming materials taught by Grimm include gelatin; however the examiner points out that independent claim 24 does not specify a wall forming material. Further, the instant claims do not exclude the encapsulation of the active agent in the microparticles nor do the claims require the bioactive to be coated on the particle. Independent claim 24 is broadly directed to spray drying wall-forming materials including the bioactive agent. Grimm teaches various method of forming the microparticles that comprise an active and a film forming material, which includes spray drying and Cohen teaches producing microparticles by spray drying. The claims do not structurally define the microparticle produced by the method and thus it is the examiner's position that Grimm in view of Cohen renders the instant claims obvious.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible

harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 24-25 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of U.S. Patent No. 6,565,885. Although the conflicting claims are not identical, they are not patentably distinct from each other because:

Instant claim 24 is directed to a method for preparing microparticles with a wall thickness of about 100-500nm , wherein said method comprises spray-drying wall-forming materials and a bioactive agent, wherein said method further comprises inclusion of a blowing agent in the feedstock for spray drying.

Instant claim 25 is directed to the method according to claim 24, wherein said blowing agent is selected from the group consisting of ammonium acetate, ammonium carbonate, and acids.

US patent is directed to a method of forming a powder comprising microstructures by spray drying comprising the steps: providing a feed stock comprising a bioactive agent, surfactant, and a blowing agent wherein said blowing agent is selected from the group consisting of fluorinated compounds, nonfluorinated oils, ammonium salts, alcohols, chloroform, ethyl acetate, acetone, nitrogen, carbon dioxide, camphor, and latex wherein the ratio of blowing

agent/surfactant is between 1.0-60 w/w; atomizing said feed stock to produce dispersed droplets; drying said droplets to form perforated microstructures comprising said bioactive agent and surfactant; and collecting said perforated microstructures. US claim 34 is directed to ammonium carbonate and camphor as the blowing agent. The method produces microparticles with the instantly claimed wall thickness. See Figure 1, which produces a microparticle with a wall thickness of 43.5 to 261 nm.

The instant application and US patent are directed to obvious and overlapping subject matter. Firstly, although the instant claims are directed to "microparticles" and US patent is directed to "perforated microstructures", these are considered obvious subject matter since the instant specification (page 25) discloses on that the blowing agent provides this perforated structure. Secondly, the instant specification discloses the use of surfactants as part material that forms the microstructures. Lastly, claim 25 is directed to ammonium carbonate or acetate as the blowing agent. Thus, the instant claims is directed to the broader scope without specifying the wall-forming material and blowing agent and US patent is directed to the narrower scope wherein the wall-forming agent is specified and the blowing agent.

Response to Arguments

Applicant request the rejection is held in abeyance until the claims are found to be allowable. The examiner maintains the rejection until a Terminal Disclaimer is filed to properly overcome the rejection.

Conclusion

All the claims are rejected at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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